



The Consequences of Untreated Iron Deficiency During Pregnancy



S. Mahadasu, S. Rao, & M. Khodamoradi

Objective This is a narrative review of recent studies, clinical trials, and national guidelines, exploring the implications of untreated iron deficiency (ID) and iron deficiency anaemia (IDA) during pregnancy.

Findings

Anaemia and PPH: Prevalence of anaemia in the UK, is estimated to be between 24% and 46%.¹ Anaemia is a well-known consequence of postpartum haemorrhage (PPH), but it is also a cause of PPH.² Compared to non-anaemic women, anemic patients tend to bleed more within a given period of time. Additionally, anaemic blood clots may be more susceptible to fibrinolysis due to the essential role red blood cells play in coagulation.³ Iron deficiency anaemia might also cause uterine atony because of raised nitric oxide as well as impaired uterine oxygenation.^{4,5} It is crucial to note that even moderate bleeding can be life-threatening in anaemic women.²

Furthermore, anaemia and thrombocytopenia even at the level between 100 and 150 × 103/μL, act synergistically in increasing the risk of PPH.⁶

Iron Deficiency and Pruritus Without a Rash: Both ID and IDA can cause generalised pruritus without a rash (GPWOR). In all cases of GPWOR, ID should be ruled out. In some cases, iron replacement leads to complete cessation of pruritus.⁷ Around 25% of pregnant women develop pruritus without progressing to Intrahepatic Cholestasis of Pregnancy.⁸

ID, IDA and Postpartum depression (PPD): Iron is an essential element for all body cells.⁹ Untreated ID during pregnancy is associated with postpartum depression (PPD). Numerous studies, including well-designed randomised controlled trials, have demonstrated a significant association between ID and the development of PPD with improvement in mood following iron repletion.¹⁰

Fetal Effects of ID in Pregnancy: Cord iron levels are reduced when mother's serum ferritin goes below 13 μg/l. IDA in pregnancy has potential implications for the future neuro-development of the infant.¹

Correspondence: m.khodamoradi@nhs.net

Diagnosis of ID:

- Serum ferritin level of <30 μg/l
- In the setting of inflammation, serum ferritin <70 μg/L.⁹

Treatment of ID: 40–80 mg every morning with checking Hb at 2–3 weeks to ensure an adequate response. Higher doses potentially increase side effects.¹

Options For Intolerance to Oral Treatment:

- Alternate day dosing
- Oral ferric maltol
- Parenteral iron

Switching to another oral iron salt is not supported by evidence.¹¹ Ferric maltol is a stable complex of ferric iron with maltol which allows ferric iron to reach the intestinal mucosa in complex form leading to more efficient uptake of elemental iron into enterocytes.¹²

Side Effects of IV Iron: The risk of anaphylactoid reactions is between 1 in 10,000 and 1 in 1,000.¹ The majority of IV-iron reactions are not IgE-mediated anaphylactic reactions.¹³

Fishbane Reaction: This occurs in about 1% of patients, characterised by arthralgias, flushing and chest tightness **without wheezing, stridor, angioedema, or hypotension.**^{9, 14}

Management:

- Immediately examine the patient to R/O anaphylactic reactions
- Stop infusion
- If patient remains stable & asymptomatic, restart the infusion after 15 minutes at ≥50% of the original rate
- Avoid administration of antihistamines or vasopressors which lead to severe haemodynamic complications¹⁵

Fishbane reactions are thought to result from the presence of labile free iron in the circulation, released from the iron–carbohydrate complex more rapidly than transferrin can bind it.^{14, 15, 16}

Conclusions: ID and IDA are common in pregnancy and are associated with increased maternal and perinatal morbidity and mortality. Addressing ID during pregnancy is vital to reduce the risk of PPH, and to mitigate broader maternal and perinatal complications. Increased awareness and timely treatment may play a key role in reducing the risk of postpartum depression.

References

- 1- Pavord S, Daru J, Prasanna N, Robinson S, Stanworth S, Gilling J; on behalf of the BSH Committee. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol. 2020 Jan;188(6):819–30. doi:10.1111/bjh.16221.
- 2- London School of Hygiene & Tropical Medicine. About WOMAN-2 – WOMAN-2 Trial [Internet]. London: LSHTM; [cited 2025 Jun 3]. Available from: <https://woman2.lshtm.ac.uk/about-woman-2/>
- 3- Walton BL, Byrnes JR, Wolberg AS. Fibrinogen, red blood cells, and factor XIII in venous thrombosis. J Thromb Haemost. 2015 Jun;13 Suppl 1(Suppl 1):S208–15. doi:10.1111/jth.12918. PMID: 26149026; PMCID: PMC5975993.
- 4- The WOMAN-2 trial collaborators. Maternal anaemia and the risk of postpartum haemorrhage: a cohort analysis of data from the WOMAN-2 trial. Lancet Glob Health. 2023 Aug;11(8):e1249–e1259. doi:10.1016/S2214-109X(23)00245-0.
- 5- Soltan MH, Ibrahim EM, Tawfik M, Hassan H, Farag F. Raised nitric oxide levels may cause atonic postpartum hemorrhage in women with anemia during pregnancy. Int J Gynaecol Obstet. 2012 Mar;116(3):197–9. doi:10.1016/j.ijgo.2011.09.017.
- 6- Kazma J, Ebner M, Whitley J, Ahmadia HK. Impact of anemia and thrombocytopenia on postpartum hemorrhage risk among women with term singleton pregnancy. J Thromb Thrombolysis. 2023 Apr;55(3):571–5. doi:10.1007/s11239-022-02756-9. PMID: 36592298.
- 7- Millington GWM, Collins A, Lovell CR, Leslie TA, Yong ASW, Morgan JD, et al. British Association of Dermatologists' guidelines for the investigation and management of generalized pruritus in adults without an underlying dermatosis, 2018. Br J Dermatol. 2018 Jan;178(1):34–60. doi:10.1111/bjd.16117.
- 8- Royal College of Obstetricians and Gynaecologists. Obstetric Cholestasis (Green-top Guideline No. 43). London: RCOG; 2022.
- 9- Lucas S, and Garg, M. (2024). Intravenous iron: an update. Intern Med J, 54: 26-34. <https://doi.org/10.1111/imj.16184>
- 10- Wassef, A., Nguyen, Q. D., & St-André, M. (2018). Anaemia and depletion of iron stores as risk factors for postpartum depression: a literature review. Journal of Psychosomatic Obstetrics & Gynecology, 40(1), 19–28. <https://doi.org/10.1080/0167482X.2018.1427725>
- 11- National Institute for Health and Care Excellence (NICE). Anaemia – iron deficiency. Clinical Knowledge Summary. Last revised August 2024. Available from: <https://cks.nice.org.uk/topics/anaemia-iron-deficiency/> 12- Schmidt C, Ahmad T, Tulassay Z, Baumgart DC, Bokemeyer B, Howaldt S, et al. Ferric maltol therapy for iron deficiency anaemia in patients with inflammatory bowel disease: long-term extension data from a Phase 3 study. Aliment Pharmacol Ther. 2016 Jul;44(1):35–44. <https://doi.org/10.1111/apt.13665>
- 13- Saebøien J, Fishbane S, Hedenius M, Howaldt S, Locatelli F, Petri S, et al. Hypersensitivity to intravenous iron: classification, terminology, mechanisms and management. Br J Pharmacol. 2015 Oct;172(21):5025–36. <https://doi.org/10.1111/bph.13268>
- 14- Caimmi S, Crisafulli G, Franceschini F, Liotti L, Bianchi A, Bottau P, Mori F, Triggiano P, Pagliarunga C, Saretta F, Giannetti A, Ricci G, Caffarelli C. Hypersensitivity to Intravenous Iron Preparations. Children (Basel). 2022 Sep 27;9(10):1473. doi: 10.3390/children9101473. PMID: 36291409; PMCID: PMC9600424.
- 15- Society for the Advancement of Blood Management (SABM). Fishbane Reaction [Internet]. SABM; [cited 2025 Jun 3]. Available from: <https://www.sabm.org/assets/pdfs/4-Fishbane-Reaction.pdf>
- 16- Lim W, Afif W, Knowles S, Lim G, Lin Y, Mothersill C, et al. Canadian expert consensus: management of hypersensitivity reactions to intravenous iron in adults. Vox Sang. 2019 Apr;114(4):363–373. doi:10.1111/vox.12773.

